

SEQUENCE LISTING

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<120> HUMANIZED ANTIBODIES THAT RECOGNIZE VEROTOXIN II AND
CELL LINE PRODUCING SAME

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<140> US 09/700851
<141> 2000-11-17

<150> WO 99/59629
<151> 1999-05-19

<150> US 60/086,570
<151> 1998-05-20

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<170> PatentIn Ver. 2.1

<210> 1
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<220>
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<223> Figure 1(A): Heavy chain variable region of mouse
antibody VTm1.1 (MuVTm1.1).

<400> 1
atg aac ttt gtg ctc agc tcg att ttc ctt gcc ctc att tta aaa gga 48
Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15

gtc cag tgt gaa gtg cag ctg gtg gag tcg ggg gga ggc tta gtg aag	96	
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys		
20	25	30

cct gga ggg ccc ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc 144
 Pro Gly Gly Pro Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
 35 40 45

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agt agt tat ggc atg tct tgg gtt cgc cag act ccg gag aag agg ctg      192
Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu
      50          55          60

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gag tgg gtc gca acc att agt act ggt ggt agt tac acc tac tac cca 240
 Glu Trp Val Ala Thr Ile Ser Thr Gly Gly Ser Tyr Thr Tyr Tyr Pro
 65 70 75 80

gac agt gtg aag ggt cga ttc acc atc tcc aga gac aat gcc aag aac 288
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
85 90 95

gcc ctg tat ctg caa atg agc agt ctg agg tct gag gac acg gcc ata 336
Ala Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile
100 105 110

tat tac tgt gca aga cgg ggg gac gca tgg ggt aac ttg gac tac tgg 384
Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp
115 120 125

ggt caa gga acc tct gtc acc gtc tcc tca 414
Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135

<210> 2
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<212> PRT
<213> Mus musculus

<220>
<223> Figure 1(A): Heavy chain variable region of mouse antibody VTm1.1 (MuVTm1.1).

<400> 2
Met Asn Phe Val Leu Ser Ser Ile Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
20 25 30

Pro Gly Gly Pro Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Gly Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu
50 55 60

Glu Trp Val Ala Thr Ile Ser Thr Gly Ser Tyr Thr Tyr Tyr Pro
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
85 90 95

Ala Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile
100 105 110

Tyr Tyr Cys Ala Arg Arg Gly Asp Ala Trp Gly Asn Leu Asp Tyr Trp
115 120 125

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135

<210> 3
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<222> (1)..(381)

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<223> Figure 1(B): Light chain variable region of mouse
VTm1.1 antibody (MuVTm1.1).

<400> 3
atg gtt ttc aca cct cag ata ctt gga ctt atg ctt ttt tgg att tca 48
Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

gcc tcc aga ggt gat gtt gtg cta act cag tct cca gcc acc ctg tct 96
Ala Ser Arg Gly Asp Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

gtg act cca gga gat agc gtc agt ctt tcc tgc agg gcc agt caa act 144
Val Thr Pro Gly Asp Ser Val Ser Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

att agc aac aac cta cac tgg tat caa cac aaa tca cat gag tct cca 192
Ile Ser Asn Asn Leu His Trp Tyr Gln His Lys Ser His Glu Ser Pro
50 55 60

agg ctt ctc atc aag tct gct tcc cag tcc atc tct ggg atc ccc tcc 240
Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser
65 70 75 80

agg ttc agt ggc agt gga tca ggg aca gat ttc act ctc agt atc aac 288
Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn
85 90 95

agt gtg gaa act gaa gat ttt gga atg tat ttc tgt caa cag agt tac 336
Ser Val Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys Gln Gln Ser Tyr
100 105 110

agc tgg ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa 381
Ser Trp Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
115 120 125

<210> 4
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<223> Figure 1(B): Light chain variable region of mouse
VTm1.1 antibody (MuVTm1.1).

<400> 4
Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
1 5 10 15

Ala Ser Arg Gly Asp Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
20 25 30

Val Thr Pro Gly Asp Ser Val Ser Leu Ser Cys Arg Ala Ser Gln Thr
35 40 45

Ile	Ser	Asn	Asn	Leu	His	Trp	Tyr	Gln	His	Lys	Ser	His	Glu	Ser	Pro
50						55					60				
Arg	Leu	Leu	Ile	Lys	Ser	Ala	Ser	Gln	Ser	Ile	Ser	Gly	Ile	Pro	Ser
65				70					75					80	
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Ser	Ile	Asn
	85					90							95		
Ser	Val	Glu	Thr	Glu	Asp	Phe	Gly	Met	Tyr	Phe	Cys	Gln	Gln	Ser	Tyr
	100					105						110			
Ser	Trp	Pro	Leu	Thr	Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys	
	115				120					125					

<210> 5
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<223> Figure 2(A): Heavy chain variable region of
humanized VTm1.1 antibody (HuVTm1.1).

<400> 5																	
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Met	Asn	Phe	Val	Leu	Ser	Ser	Ile	Phe	Leu	Ala	Leu	Ile	Leu	Lys	Gly		
1		5							10						15		
gtc	cag	tgt	gaa	gtg	caa	ctg	gtg	gag	tgc	ggg	gga	ggc	tta	gtg	cag	96	
Val	Gln	Cys	Glu	Val	Gln	Ieu	Val	Glu	Ser	Gly	Gly	Gly	Ley	Val	Gln		
				20				25					30				
cct	gga	ggg	tcc	ctg	aga	ctc	tcc	tgt	gca	gcc	tct	gga	ttc	act	ttc	144	
Pro	Gly	Gly	Ser	Leu	Arg	Ieu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe		
				35				40					45				
agt	agt	tat	ggc	atg	tct	tgg	gtt	cgc	cag	gct	ccg	ggt	aag	ggt	ctg	192	
Ser	Ser	Tyr	Gly	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Ley		
				50			55			60							
gag	tgg	gtc	gca	acc	att	agt	act	ggt	agt	tac	acc	tac	tac	cca	240		
Glu	Trp	Val	Ala	Thr	Ile	Ser	Thr	Gly	Gly	Ser	Tyr	Thr	Tyr	Tyr	Pro		
				65			70			75					80		
gac	agt	gtg	aag	ggt	cga	ttc	acc	atc	tcc	aga	gac	aat	tcc	aag	aac	288	
Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn		
				85					90				95				
acc	ctg	tat	ctg	caa	atg	aac	agt	ctg	agg	gct	gag	gac	acg	gcc	gta	336	
Thr	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val		
				100				105					110				
tat	tac	tgt	gca	aga	cgg	ggg	gac	gca	tgg	ggt	aac	ttg	gac	tac	tgg	384	

Tyr	Tyr	Cys	Ala	Arg	Arg	Gly	Asp	Ala	Trp	Gly	Asn	Leu	Asp	Tyr	Trp	
115																125
ggt	caa	gga	acc	tta	gtc	acc	gtc	tcc	tca							414
Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser							
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<210> 6																
<211> 138																
<212> PRT																
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<223> Figure 2(A): Heavy chain variable region of humanized VTm1.1 antibody (HuVTm1.1).																
<400> 6																
Met	Asn	Phe	Val	Leu	Ser	Ser	Ile	Phe	Leu	Ala	Leu	Ile	Leu	Lys	Gly	
1																15
Val	Gln	Cys	Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	
																20
																25
																30
Pro	Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	
																35
																40
																45
Ser	Ser	Tyr	Gly	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	
																50
																55
																60
Glu	Trp	Val	Ala	Thr	Ile	Ser	Thr	Gly	Ser	Tyr	Thr	Tyr	Tyr	Tyr	Pro	
																65
																70
																75
																80
Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	
																85
																90
																95
Thr	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	
																100
																105
																110
Tyr	Tyr	Cys	Ala	Arg	Arg	Gly	Asp	Ala	Trp	Gly	Asn	Leu	Asp	Tyr	Trp	
115																125
Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser							
																130
																135

<210> 7															
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<223> Figure 2(B): Light chain variable region of humanized VTm1.1 antibody (HuVTm1.1) .															
<400> 7															

atg gtt ttc aca cct cag ata ctt gga ctt atg ctt ttt tgg att tca Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser	1 5 10 15	48
gcc tcc aga ggt gaa att gtg cta act cag tct cca gcc acc ctg tct Ala Ser Arg Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser	20 25 30	96
gtg tct cca gga gaa aga gcc act ctt tcc tgc agg gcc agt caa act Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr	35 40 45	144
att agc aac aac cta cac tgg tat caa caa aaa cca ggt cag gct cca Ile Ser Asn Asn Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro	50 55 60	192
agg ctt ctc atc aag tct gct tcc cag tcc atc tct ggg ata ccc gcc Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ala	65 70 75 80	240
agg ttc agt ggc agt gga tca ggg aca gat ttc act ctc act atc agc Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser	85 90 95	288
agt ctg gaa tct gaa gat ttt gca gtg tat tac tgt caa cag agt tac Ser Leu Glu Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr	100 105 110	336
agt tgg ccg ctc acg ttc ggt caa ggg acc aag gtg gag atc aaa Ser Trp Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	115 120 125	381

<210> 8
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<213> Mus musculus

<220>
<223> Figure 2(B): Light chain variable region of
humanized VTm1.1 antibody (HuVTm1.1) .

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<400> 8
Met Val Phe Thr Pro Gln Ile Leu Gly Leu Met Leu Phe Trp Ile Ser
   1           5           10          15

Ala Ser Arg Gly Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
   20          25          30

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr
   35          40          45

Ile Ser Asn Asn Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
   50          55          60

Arg Leu Leu Ile Lys Ser Ala Ser Gln Ser Ile Ser Gly Ile Pro Ala
   65          70          75          80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
   85          90          95

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Ser Leu Glu Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Tyr
100 105 110

Ser Trp Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
115 120 125

<210> 9

<211> 123

<212> PRT

<213> Homo sapiens

<220>

<223> heavy chain variable region of the GF4/1.1 antibody

<400> 9

Glu Val Gln Val Leu Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr
20 25 30
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Gly Ile Ser Ala Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Pro Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Asp Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Lys Gly Gly Arg Gln Trp Val Val Leu Gly Tyr Phe Phe Asp Ser
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 10

<211> 110

<212> PRT

<213> Homo sapiens

<220>

<223> light chain variable region of the GF4/1.1 antibody

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Glu Ile Leu Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Leu Tyr Tyr Cys His Glu Tyr Asn Gly Trp Pro Pro
85 90 95
Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr
100 105 110